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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,548	03/15/2002	Jihoon Chang	58049-00002	6655

7590 10/21/2003

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EXAMINER	
HADDAD, MAHER M	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 10/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,548	CHANG ET AL.	
	Examiner	Art Unit	
	Maher M. Haddad	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 August 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4 and 18-33* is/are pending in the application.

4a) Of the above claim(s) *18,19 and 24-33* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 20-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 8/14/03
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 8/14/03, is acknowledged.

2. Claims 1-4 and 18-33 are pending.

3. Claims 18-19 and 24-33 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

4. Claims 1-4 and 20-23 are under consideration in the instant application as they read on the LK68 protein comprising amino acid sequence of human apolipoprotein(a) kringle domains IV36, IV37 and V38 and LK68 protein single Kringles domains.

5. In view of the amendment filed on 8/14/03, only the following rejection remain.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4 and 20-23 are rejected under 35 U.S.C. 112, first paragraph, the specification does not reasonably provide **enablement** for how to use a recombinant LK6, LK7, LK8 or LK68 polypeptides consisting of SEQ ID NO: 4, 6, 8, 2, respectively and a composition thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with this claim for the same reasons set forth in the previous Office Action mailed 4/09/03.

Applicant's arguments, filed 6/12/03 8/14/03 have been fully considered, but have not been found convincing

Applicant asserts that the isolated kringle domains LK6, LK7, LK8 and their combination LK68 provide an unexpected result of inhibiting capillary development, inhibiting endothelial cell proliferation and migration and suppressing tumor growth, which are all related to the inhibition of angiogenesis. Applicant submits that the specification fully enables the invention and shows possession of these polypeptide.

While the specification on pages 18-19, under example 6-1 and 6-2, discloses that such the growth of LLC primary tumors was potently suppressed by systemic LK68 therapy and the LK68 treated A549 tumors were 57.5% smaller than tumors in control animals. However, the state of the art does not appear to recognize the polypeptides of SEQ ID NO:2, 4, 6 and 8 would function in a method of inhibiting angiogenesis in a malignant condition. In an article (The Scientist 16:33, 2002, Learning from Angiogenesis Trial Failures) Fogarty M writes that 12 recent failures of Phase III angiogenesis trial failures have bashed some scientists' hopes for success. Furthermore, in the same article Claude Hariton indicates that "Multimodality is

definitely the future in angiogenesis and antiangiogenic drug development because there is a dependency of several complex processes in angiogenesis. Shutting one door won't allow the drug to solve the problem. You have to shut, if possible, all the doors by which the vessels will grow around the tumor". Therefore, it is not clear that the skilled artisan could predict the efficacy of any "kringle domains" exemplified in the specification. *In re Fisher*, 166 USPQ 18 indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

The current list of molecules identified as "anti-angiogenic" is extensive, with significant diversity in their structural, chemical and biological properties (see Fan et al., Trends in Pharm. Sci. 16(2):57-66, page 57, column 2 and page 65, column 1, first paragraph in particular). Similarity, Wallace (Drug Discovery Today, 3(10):433-4) teach that while there are ongoing clinical trials for the different categories of anti-angiogenic agents, we still have a limited understanding of the process of angiogenesis such that our ability to predict the efficacy of new agents is limited to the in vivo tumor growth animal models which often show promise in mice but are found ineffective in humans (page 433 column 2 in particular).

Thus faced with failures of Phase III angiogenesis trial failures, undue experimentation would be required of the skilled artisan to determine the "anti-angiogenic" effects of LK6, LK7, Lk8, LK68 polypeptides on a subject in view of the instant disclosure.

In view of the absence of a specific and detailed description in Applicant's specification of how to effectively use the LK6, LK7, Lk8, LK68 polypeptides as claimed, and absence of working examples providing evidence which is reasonably predictive that the claimed LK6, LK7, Lk8, LK68 polypeptides are effective for human use, and the lack of predictability in the art at the time the invention was made, an undue amount of experimentation would be required to practice the claimed methods with a reasonable expectation of success.

7. No claim is allowed.

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Maher Haddad, whose telephone number is (703) 306-3472. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 872-9307.

Maher Haddad, Ph.D.
Patent Examiner
Technology Center 1600
October 20, 2003

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600